PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application Serial No. 06/659,339

Filed: October 10, 1984

CANCELLATION OF
PETITION FOR ACCESS TO PATENT APPLICATION
PURSUANT TO 37 C.F.R. 1.14(a) AND (e)

Nutley, New Jersey 07110
July 24, 1996

Assistant Commissioner for Patents
Washington, D.C. 20231

Attn: Special Program Law Office
Petition Information
Crystal Park One
Suite 520

Sir:

This paper is submitted to cancel the Petition For Access to Patent Application pursuant to 37 CFR 1.14(e)(1), which was mailed to the U.S. Patent and Trademark Office on June 11, 1996 by Catherine R. Smith. Enclosed is a copy of this Petition.

The undersigned attorney, on behalf of Ms. Catherine R. Smith who is on vacation, is requesting cancellation of this Petition. The undersigned attorney is the supervisor of Catherine R. Smith and together with Ms. Smith is employed in the Patent Law Department of Hoffmann-La Roche Inc., 240 Kingsland Street, Nutley, NJ 07110.

Betty Byrd, Ina

PATENT STENOGRAPHY
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AREA CODE 703-415-1224
FAX 703-413-2827

July 24, 1996

For: Mr. Hoffman
Deputy Assistant Commissioner's Office

Re: Abandoned Application Serial No. 06/659,339 - CHANG
(USP 4,774,175)

I am FAXing herewith the cancellation of the Petition which was filed and directed to your department. Please let me know when this file will be available for me to copy same. Thanks. My number is 415-1224.

Betty Byrd

CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this paper (along with any paper referred to as being transmitted therewith) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Assistant Commissioner for Patents, Washington, D.C. 20231.

Catherine R. Smith
(Print Name)

Date: July 11, 1996

(Signature)

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PETITIONS OFFICE

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Sir:

Pursuant to 37 CFR 1.14(e)(1), the undersigned and appointees hereby petition for access to the above captioned patent application, to inspect and make copies thereof for the reasons set forth below.

The above patent application has been incorporated by reference in an issued U.S. Patent. U.S. Patent No. 4,774,175 issued September 27, 1988. A copy of the title page and page

DEPOSIT ACCOUNT
NO. 08-0525
OUR ORDER NO. 2561

encompassing columns 3 and 4 of that patent are attached hereto. In this regard attention is directed to column 4, lines 6 through 12, especially lines 8 through 9.

By incorporating by reference the above patent application into U.S. Patent No. 4,774,175, the right of confidentiality secured by 35 USC 122 has been waived with regard to the above application. (In re Yang, 177 USPQ 88 (Pat. Off. Sol. 1973); In re Gallo, 231 USPQ 496 (Commr. Pat. 1986; MPEP §103). Accordingly, the undersigned respectfully requests access to the captioned patent application as originally filed and to the file history thereof.

The undersigned submits that the requirements of 37 CFR 1.14(e)(1) have been met and respectfully requests that the present petition be granted.

The Assistant Commissioner of Patents and Trademarks is hereby authorized to charge the required petition fee of $130.00, 37 CFR 1.17(l), and any other related fees to this petition or to credit any overpayment to Deposit Account No. 08-2525.

Respectfully submitted,

Attorney of Applicant(s)
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24060
Encl.

United States Patent [19]
Chang et al.

[11] Patent Number: 4,774,175
[45] Date of Patent: Sep. 27, 1988

[54] IMMUNOCHEMICAL METHODS FOR THE DETECTION OF ANTIBODY AGAINST HTLV-III

[75] Inventors: Tse W. Chang, Paoli; Ikunobiu Kato, Exton; Prasad Chandra; Nancy T. Chang, both of Paoli, all of Pa.

[73] Assignee: Centocor, Inc., Malvern, Pa.

[21] Appl. No.: 707,066

[22] Filed: Mar. 1, 1985

[51] Int. Cl.[4] C12Q 1/70; C01N 33/544

[52] U.S. Cl. 435/5; 435/7; 435/180; 435/805; 436/518; 436/528; 436/531; 436/811; 530/324

[58] Field of Search 435/5, 7, 180, 805; 530/324; 436/518, 528, 531, 811

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Primary Examiner—Christine M. Nucker
Attorney, Agent, or Firm—Hamilton, Brook, Smith & Reynolds

[57] ABSTRACT

Gene segments of human T cell lymphotropic virus type III (HTLV-III) were expressed in *E. coli* as peptides that are reactive with sera from patients with acquired immune deficiency syndrome (AIDS). Among recombinant peptides one designated HTLV-III polypeptide 121, contained 85 amino acid residues encoded by a gene segment in the env-lor region of the HTLV-III genome. The polypeptide is strongly reactive with AIDS patient sera. The peptide produced and purified as a fusion protein on a large scale. Solid phase immunoassays employing this recombinant peptide as an immunosorbent can reliably and reproducibly detect antibodies in sera of patients with HTLV-III infection. In two representative serum panels, the assay detected the presence of antibodies in 120 of 121 sera from patients with AIDS or AIDS-related complex (ARC), and only in 1 of 92 normal controls. Based upon HTLV-III polypeptide 121 as immunoreactive agent, sensitive and specific immunoassays for HTLV-III infection have been developed.

15 Claims, 2 Drawing Sheets

The polypeptide can be used in assays of various types including immunometric assays and antigen-sandwich assays. A preferred type of assay is a solid phase immunometric (double antibody) assay. HTLV-III polypeptide 121 is immobilized by attaching it to solid phase to form an antigen immunoadsorbent. The immunoadsorbent is used to adsorb anti-HTLV-III antibody from a sample of the biological fluid. The adsorbed anti-HTLV-III antibody is detected with an anti-(human IgG) antibody which is labeled radioisotopically, enzymatically, fluorometrically or in other ways. This second antibody, directed generally against human IgG, binds to anti-HTLV-III antibody adsorbed to the immunoadsorbent and produces a detectable signal which can be evaluated as an indication of the presence of anti-HTLV-III antibody in the sample.

The immunochemical assays employing HTLV-III polypeptide 121 provide several advantages over those based on the whole virus. Assays based upon HTLV-III polypeptide 121 eliminate the need to grow large quantity of the infectious virus. This alleviates the risk associated with this process. Additionally, assay reagents based upon the HTLV-III antigen rather than the whole virus will help mitigate the real or perceived risk of contracting AIDS by technicians who perform the assay.

In performance, assays employing HTLV-III polypeptide 121 are excellent. HTLV-III polypeptide 121 is a single, well defined component which provides a reproducible assay exhibiting less variab r. For example, in solid phase assays, background level associated with the immunoadsorbent is low. Further, the assays are surprisingly highly sensitive and specific. Because the polypeptide presumably exhibits far fewer epitopes than the whole virus and consequently should be reactive with a smaller fraction of the antibody against the virion, the high sensitivity and specificity was not expected. In the immunometric assay, the polypeptide detected the presence of anti-HTLV-III antibody in 99% of sera of patients with AIDS and ARC. The very high specificity of the assay suggests that HTLV-III polypeptide 121 is derived from a highly antigenic portion of the virion and that antibody against the antigen is evoked in virtually all instances of HTLV-III infection. These performance characteristics provide for highly accurate screening of blood and other bodily fluids for the presence of HTLV-III and for greater precision in the diagnosis of AIDS.

Because of the apparent strong antigenicity of HTLV-III polypeptide 121, it could be used as a vaccine against the virus.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a comparison between solid phase immunoadsorbents using recombinant HTLV-III antigen, polypeptide 121, and inactivated, disrupted HTLV-III as antigen.

FIG. 2 shows assay results on sera samples from patients with AIDS or ARC and from normal individuals with immunoradiometric assays employing recombinant HTLV-III polypeptide 121 as a solid-phase immunoadsorbent.

BEST MODE OF CARRYING OUT THE INVENTION

HTLV-III polypeptide 121 was expressed and identified by a shotgun cloning procedure. This procedure is described in detail in U.S. patent application Ser. No. 659,339, which is incorporated by reference herein. For completeness, the procedure is outlined here and described in further detail in the Exemplification Section below.

Cloned HTLV-III DNA was broken into fragments of approximately 500 base pairs in length and inserted into the "open reading frame" (ORF) cloning and expression vector pMR100. The inserted DNA was expressed in *E. coli* transformants as tripartite fusion proteins, consisting of an HTLV-III polypeptide fused to λCI protein at its N-terminal and beta-galactosidase at its C-terminal. About 300 clones were found to express beta-galactosidase activity indicating expression of the tripartite fusion proteins. AIDS patient sera containing anti-HTLV-III antibodies were used to screen for fusion proteins that were immunoreactive. Among twenty clones which produced proteins reactive with the AIDS sera, one clone, designated clone #121, expressed a fusion protein which was immunoreactive with all AIDS patient sera examined (24/24). The highly immunoreactive protein produced by this clone was selected for further study.

The HTLV-III DNA segment of clone 121 was excised from pMR100 and sequenced by the Sanger technique. The nucleotide sequence is as follows:

ATT	GAG	GCG	CAA	CAG	CAT	CTG	TTG	CAA	CTC	ACA	GTC	TGC
GGC	ATC	AAG	CAG	GTC	CAG	GCA	AGA	ATC	CTG	GGT	GTG	GAA
AGA	TAC	CTA	AAG	GAT	CAA	CAG	CTC	CTG	GGG	ATT	TGG	GGT
TGC	TCT	GGA	AAA	CTC	ATT	TGC	ACC	ACT	GCT	GTG	CCT	TGG
AAT	GCT	ACT	TGG	AGT	AAT	AAA	TCT	CTG	GAA	CAG	ATT	TGG
AAT	AAC	ATG	ACC	TGG	ATG	GAG	TGG	GAC	AGA	GAA	ATT	AAC
AAT	TAC	ACA	AGC	TTA								

Based upon the DNA sequence, the putative amino acid sequence of the HTLV-III polypeptide could be assigned. This sequence is given below.

Ile	Glu	Ala	Gln	Gln	His	Leu	Leu	Gln	Leu
Thr	Val	Trp	Gly	Ile	Lys	Gln	Leu	Gln	Ala
Arg	Ile	Leu	Ala	Val	Glu	Arg	Tyr	Leu	Lys
Asp	Gln	Gln	Leu	Leu	Gly	Ile	Trp	Gly	Cys
Ser	Gly	Lys	Leu	Ile	Cys	Thr	Thr	Ala	Val
Pro	Trp	Asn	Ala	Ser	Trp	Ser	Asn	Lys	Ser
Leu	Glu	Gln	Ile	Trp	Asn	Asn	Met	Thr	Trp
Met	Glu	Trp	Asp	Arg	Glu	Ile	Asn	Asn	Tyr
Thr	Ser	Leu							

The pMR100 tripartite fusion protein synthesized by clone 121 was difficult to purify in sufficient quantity for sera screening because the expression level was low (approximately 1.0% of total cellular protein) and the protein was insoluble in conventional extractive buffer (probably due to the existence of 23 half-cystine residues). In order to enhance expression the HTLV-III polypeptide in *E. coli* the HTLV III segment of clone 121 was cloned into a beta-glucuronidase expression vector. *E. coli* transformed with the recombinant vector expressed a 15 Kd fusion protein with short fusion partners at both ends (41 amino acids of *E. coli* the 83 amino acid residues encoding by HTLV-III polypeptide and 13 amino acid residues encoded by a multiple cloning